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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,035	09/22/2003	Dominic P. Behan	AREN-005CON (5.US10.CON)	2177

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EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	
MAIL DATE	**DELIVERY MODE**
12/01/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,035	BEHAN ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2010 and 13 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8-10 and 20-25* is/are pending in the application.

4a) Of the above claim(s) *9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8,10 and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 01/11/2010 has been entered. Claims 1-3, 8-10, and 20-25 are pending.

In response to Requirement for Restriction/Election mailed on 05/13/2010, Applicant's election with traverse of Group I (claims 1-3, 8, 10, 20-25) in the reply filed on 11/11/2010 is acknowledged. The traversal is on the ground(s) that it would not be unduely burdensome to perform a search on all of the claims together in the present application. Applicants argue that the full scope of the claims has already been examined on the merits. This is not found persuasive because the instant claims encompass nine different orphan GPCR which are represented by nine SEQ ID NOS and each orphan GPCR requires a separate search and consideration. Search and examination of more than one orphan GPCR places an undue burden on the examiner. Thus, the requirement is still deemed proper and is therefore made FINAL.

Accordingly, Claims 1-3, 8, 10, and 20-25 are under consideration. Claim 9 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/11/2010.

Withdrawn Objections and/or Rejections

The rejection of claims 1-3, 8-10 and 20-21 under 35 U.S.C. 103(a) as being unpatentable over Seifert et al (J. Biol.. Chem, 1998, Vol 273, No. 9, pages 5109-5116 in view of Scheer et al (J. of receptor and Signal Transduction Research, 1997, Vol 17, pages 57-73) and further in view of Song et al (Genomic 1996, Vol.28, pages 347-349), Bertin et al (Proc. Natl. Acad. Sci. USA, 1994, Vol.91, pages 8827-8831) and Wise et al (J. Biol. Chem, 1997, Vol 272, No. 39, page 24673-24678) is withdrawn to set forth a new rejection.

Claim Rejections under 35 USC § 101 and 112, 1st paragraph

(i). 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

(ii). Claims 1-3, 8, 10, and 20-25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. A specific and substantial utility is one that is particular to the subject

matter claimed and that identifies a "real world" context of use for the claimed invention which does not require further research.

Claims 1-3, 8, 10, and 20-25 are drawn to a method for directly identifying an agonist or inverse agonist of an endogenous, constitutively active G protein coupled orphan receptor using a GPCR fusion protein comprising an endogenous, constitutively active G protein coupled orphan receptor and a G protein, The utility analysis for the claimed methods is based upon the utility of the agonists and antagonists screened by the method. Since neither the prior art nor the specification discloses the biological functions of the orphan G protein coupled receptor GPR3 and a patentable utility of the agonists and antagonists, the claimed method does not have a patentable utility.

First, an orphan cell surface receptor, such as GPR3, has no known ligand and is not necessarily linked to any known biological functions, any known diseases or medical conditions, there is no specific and substantial utility for an orphan cell surface receptor and thus for a method of identifying an agonist or inverse agonist using the orphan receptor. It clearly requires further research for an artisan to confirm a "real world" context of use, that is, to determine the biological functions of the orphan cell surface receptor used in the screening method of the present invention. See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Second, MPEP§2107.01 states that many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds). MPEP further states that an assessment that focuses on whether an invention is useful only in a research setting thus does not address whether an invention is useful in a patent sense. Instead, Office personal must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm. Labels such as "research tool" are not helpful in determining if an applicant has identified a specific and substantial utility for the invention.

Furthermore, MPEP§2107.01 clearly lists that a method of assaying for or identifying a material that itself has no specific and/or substantial utility does not have a specific and substantial utility.

(iii). Claims 1-3, 8, 10, and 20-25 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(iv). Response to Applicants' argument

The following response to Applicants' argument is based upon Applicants' election of the orphan GPCR, GPR3.

Beginning at the bottom of page 4 of Applicants response filed on 01/11/2010, Applicants argue that the specification shows that the expression of the orphan receptor GPR3 is higher in brain biopsy from subjects suffering from epilepsy as compared with control tissue. Applicants argue that this disease-specific expression pattern provides the impetus for screening for candidate agonist/inverse agonist compounds of GPR3. Applicants' argument has been fully considered, but is not deemed to be persuasive for because a higher expression level in brain biopsy tissue from subjects suffering from epilepsy as compared with control tissue does not establish a causal link between the GPR3 and epilepsy and does not provide a patentable utility for the agonist of GPR3. Likewise, the impetus for screening for candidate agonist/inverse agonist compounds of GPR3 does not provide a specific and substantial utility for an agonist/inverse agonist of the GPR3 to be screened because an orphan cell surface receptor, such as GPR3, has no known ligands and is not necessarily linked to any known biological functions, any known diseases or medical conditions, it clearly requires further research for an artisan to confirm a "real world" context of use, that is, to determine the biological functions of the orphan cell surface receptor and thus the agonists/inverse agonists.

At the 3rd paragraph of page 5 of Applicants response filed on 01/11/2010, Applicants' argue that Example 11 describes the identification of an inverse agonist of GPR3. This is not persuasive because the screening method itself does not provide a specific and substantial utility for an inverse agonist of GPR3.

At the bottom of page 5, Applicants argue that examples of orphan GPCR with known functional activity have been described in the art. This is not persuasive because there are no references on the record that document the functional activities of orphan GPR3.

At the 4th paragraph of page 6, Applicants argue that a person skilled in the art would not make the effort to screen an orphan GPCR if they did not have some reasons to do so. Applicants argue that the claimed assay has a specific and substantial 'real world" use because it allows a user to identify, from a library of candidates, specific compounds that have a defined modulatory activity for an orphan GPCR of interest to them, regardless of the reason. This is not persuasive for the reasons above.

Beginning at the last paragraph of page 6, Applicants continue argue that the utility of the claimed invention was analogous to the utility of the PCR. This is not persuasive because MPEP§2107.01 clearly lists that a method of assaying for or identifying a material that itself has no specific and/or substantial utility does not have a specific and substantial utility.

Beginning at the last paragraph of page 7, Applicants argue that the claims of U.S. Patent No. 5,462,856 are not limited to a particular GPCR, as knowledge of the sequence or function of the screened GPCR is not necessary to the screening method. This is not persuasive because it is well settled that each case is prosecuted on its own merits.

At the 2nd paragraph of page 8, Applicants cite MPEP 2107.01 (c) and argue that inventions used in a research or laboratory setting, including screening assays as claimed in the present invention, have a clear, specific and unquestionable utility provided they have a specifically identified substantial utility. This is not persuasive because MPEP§2107.01 clearly lists that a method of assaying for or identifying a material that itself has no specific and/or substantial utility does not have a specific and substantial utility.

Claim Rejections under 35 U.S.C. 103 (a)

(i). The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(ii). Claims 1-3, 8, 10, and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (U.S. Patent No. 5,998,164, Dec. 7, 1999; 102 (e) date: June

6, 1995) in view of Seifert et al (J. Biol. Chem. 273: 5109-5116, February 27, 1998) and Eggerick et al. (Biochem. J. 309:837-843, 1995).

Li et al. teach a method of screening for an agonist of an orphan G protein-coupled receptor GPR3, comprising providing cells expressing the receptor, contacting the expressed receptor with a test compound to observe stimulation or inhibition of a functional response, and determining whether the test compound activates the receptor (column 11, the 4th paragraph to the 8th paragraph). The cells expressing the receptor include cells from mammals (column 11, line 39). Li et al. further teach formulation of a pharmaceutical composition comprising an agonist of GPR3 (column 13, the 7th paragraph).

Li et al. do not teach (i). a GPCR fusion protein comprising an endogenous, constitutively active orphan G protein coupled receptor and a G protein used in the instantly claimed method; and (ii). screening for an inverse agonist.

Seifert et al. teach a method of determining effects of an agonist or an inverse agonist of β_2AR on GTPase and adenylyl cyclase activity in cells expressing a fusion protein comprising β_2AR and Gsα (β_2AR Gsα; see Abstract; Figures 2 and 3). Seifert et al. teach that fusion of β_2AR to Gsα promotes efficient coupling (Abstract).

Eggerick et al. teach that GPR3 is an endogenous, constitutively active orphan G

protein coupled receptor. Specifically, GPR3 is Gs-activating orphan receptor and constitutively activates adenylate cyclase (see, e.g., Abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Li et al. to identify an agonist or inverse agonist of orphan GPR3 using a GPCR fusion protein comprising GPR3 and a Gs protein with a reasonable expectation of success. One would have been motivated to do so because such a fusion protein promotes efficient coupling as taught by Seifert et al. (see e.g., Abstract).

Claim Rejections under Obviousness-Type Double Patenting

(i). The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(ii). Claims 1-3, 10, and 20 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,653,086. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Claims 1-3, 10, and 20 of the instant application are drawn to a method for directly identifying an agonist or inverse agonist of an endogenous, constitutively active G protein coupled orphan receptor using a GPCR fusion protein comprising an endogenous, constitutively active G protein coupled orphan receptor and a G protein, whereas claims 1-3 of U.S. Patent No. 6,653,086 is drawn to the same method except that a GPCR fusion protein comprising an endogenous, constitutively active G protein coupled orphan receptor and a Gsα protein. Therefore, the patented claims are related to the instant claims as species to genus with respect to G protein. A patented species (an endogenous, constitutively active G protein coupled orphan receptor and a Gsα protein) renders its genus (a GPCR fusion protein comprising an endogenous, constitutively active G protein coupled orphan receptor and a G protein) obvious and thus anticipates the genus.

Claims Objections

Claims 1-3, 8, 10, 20, 21, and 23-25 are objected to because they recite non-elected orphan GPCRs. Appropriate correction is required.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.
November 29, 2010